REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining in this application be allowed.

Claims 1 and 35–59 are pending in the present application. Claims 46–56, 58, and 59 were rejected as discussed below. Claims 2–34 are cancelled without prejudice to further prosecution in a related application, such as a continuation, continuation-in-part, divisional, or other related application.

The Applicants acknowledge the Examiner's determination that claims 1, 35–45, and 57 are allowed.

The Examiner also requested that the Applicants submit a supplemental IDS including references to provisional U.S. Patent Application Serial No. 60/022,890 and U.S. Patent Application Serial No. 08/821,825. The supplemental IDS is submitted herewith.

Rejections Under 35 U.S.C. § 112

The Examiner rejected claims 46–56, 58, 59 under 35 U.S.C. § 112 (first paragraph) as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Office Action mailed April 23, 2004, at page 2. In particular, the Examiner asserted that a review of various publications cited by the Examiner demonstrated that: "(a) structure/activity relationships in VLA-4 antagonism are unpredictable, and (b) treatment of inflammatory conditions is unpredictable as well," *Id.* at 3; and, furthermore, that "[n]o correlation has been established between [compound activity], and successful treatment of any ... diseases." *Id.* at 5. The Examiner concluded that "[c]learly 'undue experimentation' would be required" before one of skill in the art could practice invention described by the rejected claims. *Id.* at 7. This rejection is respectfully traversed in view of the following remarks.

The Applicants note initially that "[a]ll questions of enablement are evaluated against the claimed subject matter." M.P.E.P. § 2164.08 at 2100-197 (8th ed., 2nd rev. 2004). The Examiner must first "determine how broad the claim is with respect to the disclosure. The entire claim must be considered." *Id.* at 2100-198. Then, "the Examiner must determine if one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation." *Id.* However, "[a] patent need not teach, and preferably omits, what is well known in the art." *Id.* at 2100-197 (citations omitted). Furthermore, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. ... The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." M.P.E.P. § 2164.01 at 2100-185 (8th ed., 2nd rev. May, 2004) (citations omitted).

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'." M.P.E.P. § 2164.01(a) at 2100-185. The Applicants note that the Examiner lists the same exemplary factors recited in M.P.E.P. § 2164.01(a). Office Action mailed April 23, 2004, at page 5. However, the Applicants respectfully note that the M.P.E.P. cautions that "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others." M.P.E.P. § 2164.01(b) at 2100-186 (8th ed., 2nd rev. May, 2004). A conclusion that a disclosure does not satisfy the requirements of 35 U.S.C. § 112 must be "reached by weighing all the above noted factual considerations." *Id.*

The Applicants note that the rejected claims recited either a pharmaceutical composition comprising a therapeutically effective amount of a compound of the invention (claims 46–56) or a method for treating an inflammatory condition in a mammalian patient that is mediated by VLA-4, which comprises administering to the patient a therapeutically effective amount of a compound of claim 46 or claim 47 (claims 58 and 59). Claim 59 depends from claim 58 and further recites specific diseases. Thus, the Applicants respectfully submit that M.P.E.P.

§ 2164.08 requires the evaluation of enablement must relate to claim limitations of making a pharmaceutical composition having therapeutically effective amount of a compound of the invention or administering a therapeutically effective amount of such a pharmaceutical composition to a mammalian patient.

In addition, the Applicants note that the level of skill in the art is very high, typically including workers with doctorate and post-doctorate qualifications in medicinal chemistry, pharmacology, and medicine. Furthermore, those of skill in these arts were well-familiar with the possibility that a great quantity of complex, but routine, work may be required to determine pharmaceutical compositions and the delivery of such to patients on the filing date of the instant application. Examples of this familiarity can be found in the literature available commonly at the time the instant application was filed, and include *Remington's Pharmaceutical Sciences* (17^{th} ed., 1985), which is cited at page 168, lines 24 and 25, of the specification. In addition, numerous exemplary formulations and uses are described in the Specification at pages 153–170 provide further guidance to those of skill in the relevant arts.

The Applicants agree that the Examiner has presented various abstracts and summaries purporting to show that the prior art has found that certain compounds lack structure-activity relationships with respect to VLA-4 and that certain treatments for diseases involving VLA-4 activity are unpredictable. Office Action mailed April 23, 2004, at 3–4 and 5–7. However, the Applicants respectfully submit that the cited references refer to compounds that are completely different in structure from those recited in the pending claims. Furthermore, the rejected claims do not recite any limitations related to structure-activity relationships or predicting the viability of treatment methods. Thus, the rejections do not related to the limitations recited in the rejected claims, and, therefore, the rejections fail to meet the requirements set forth in M.P.E.P. § 2164.08. The Applicants thus respectfully request that the rejections should be withdrawn on these grounds alone.

Furthermore, the Applicants cannot find any evidence or argument from the Examiner that the cited references would reasonably demonstrate that one of ordinary skill in the relevant

arts would face *undue* experimentation in practicing the claimed invention. As noted in M.P.E.P. §§ 2164(a) and (b), *all* of the recited factors must be considered when determining enablement, including the guidance provided by the Applicants' disclosure. No one factor alone controls the determination of enablement. In particular, as noted above, the level of skill in the field of the invention is quite high, and those of skill are quite familiar with the degree of *routine* work that may be required to determine appropriate concentrations and doses as recited by the rejected claims. These factors must be weighed against the Examiner's assertions.

The Applicants respectfully submit that the alleged failing of the prior art to identify structure-activity relationships among compounds unrelated to the claimed compounds and provide predictable therapies that do not use the claimed compounds does not demonstrate that *undue* experimentation would be require by those of skill in the relevant arts to practice the invention in view of the high level of skill and the degree of complex, routine work common the relevant arts. The Applicants therefore respectfully submit that the Examiner's proffered demonstrations of unpredictability to reject claims 46–46, 58, and 59 as lacking enablement do not meet the standards set forth in the M.P.E.P. Again, the Applicants respectfully request withdrawal of these rejections.

CONCLUSION

The Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone (415-438-6454) if a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date July 23, 2004

By _____

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